III. REMARKS

1. STATUS OF THE CLAIMS

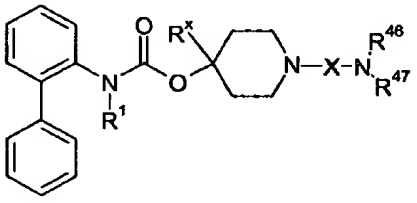
Claims 1, 4, 10-14, 18, 19, 21, 28-31, 34, 36-39, 41-45, 47 and 51are pending and stand rejected.

2. REJECTION UNDER 35 U.S.C. §103(a), OVER TAKEUCHI

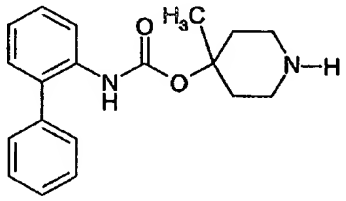
Claims 1, 4, 10-14, 18, 19, 21, 28-31, 34, 36-39, 41-45, 47 and 51 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Takeuchi, EP 0747355 (hereinafter "Takeuchi").

Takeuchi is cited for teaching carbamate compounds corresponding to the formula recited in Claim 1. The Examiner opines that one of ordinary skill in the art would be motivated to prepare compounds structurally similar to those recited in Applicants' claims in the expectation of obtaining useful compounds having muscarinic receptor antagonizing properties since structurally similar compounds are expected to have similar properties. The Examiner goes on to state that the level of skill in the art is further reflected in *In re Lohr* 137 U.S.P.Q. 548 at 549 (CCPA 1963) and in *In re Payne* 204 U.S.P.Q. 249 at 254 (CCPA 1979).

The compound recited in Claim 1 has the following structure:

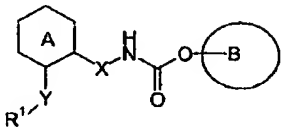


where R^x is alkyl, alkenyl, or alkynyl (i.e., a non-hydrogen substituent) and the compound of independent Claim 51 has the structure:

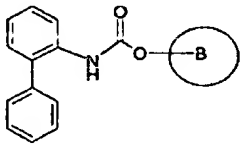


Neither of these structures is suggested by the Takeuchi teaching.

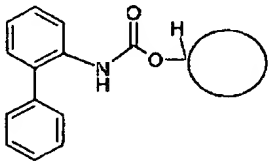
Takeuchi describes the structure:



If one were to select A as benzene, R^1 as phenyl, and X and Y as bonds, the Takeuchi structure would be:

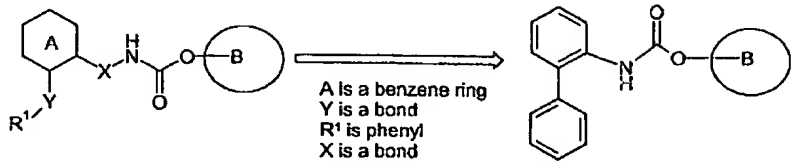


As can be seen from this structure, one distinction between the Takeuchi teaching and the claimed invention is that Takeuchi does not teach or suggest a substituent that is equivalent to the non-hydrogen R^x substituent of the claimed compounds. In all of the Takeuchi compounds, the carbon atom in the "B" ring that is linked to the carbamate moiety has a hydrogen substituent as depicted below:

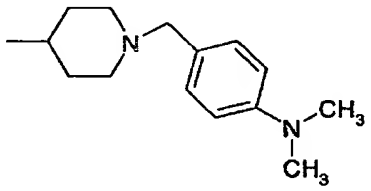


Instead of a hydrogen, the claimed compounds all recite an R^x substituent that is an alkyl, alkenyl, or alkynyl moiety, each optionally substituted with 1 to 5 alkoxy or fluoro substituents. There is nothing in Takeuchi to suggest a non-hydrogen moiety at this position, nor is there any suggestion that such a modification could be made and still maintain the desired muscarinic antagonist activity.

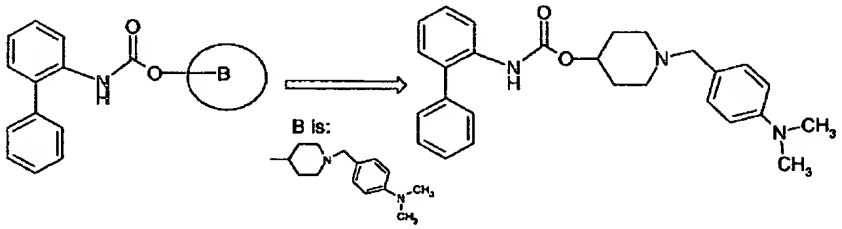
Although the Examiner makes specific reference to the compound depicted at page 47, in Example 21 of the Takeuchi reference, this compound is very different from that depicted in the claims. In Example 21, A is a benzene ring, Y is a bond, R^1 is phenyl, and X is a bond, which can be shown as follows:



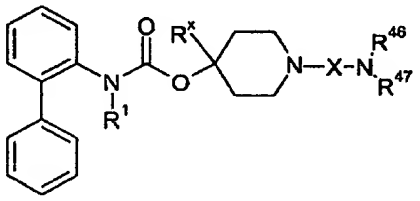
The "B" moiety in Takeuchi is defined as being "a nitrogen-containing saturated hetero-ring which may have a substituent on the nitrogen atom and which may have cross-linking." In Example 21, the B moiety is:



i.e., B is a piperidinyl group with a phenyl-dimethylamine substituent on the nitrogen. Therefore, the structure of the compound of Takeuchi's Example 21 is:



This structure does not correspond to the structure recited in claim 1:



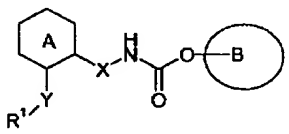
First, as noted above, the Takeuchi has no corresponding non-hydrogen R^x moiety. Second, the linker between the piperidine and the amine in Takeuchi's Example 21 is -CH_2-phenylene-. This does not fit within the definition of X in the recited claims. Briefly, X is defined as being alkylene (optionally substituted with -OH or where carbon atom(s) have been replaced by oxygen) or -alkylene-phenylene-alkylene- (optionally substituted with -Cl or -F

groups). The Takeuchi linker, -CH_2-phenylene-, is neither an alkylene group nor an -alkylene-phenylene-alkylene- group. Thus, in Takeuchi, the -$NR^{46}R^{47}$ moiety is directly linked to the phenyl group, while Applicants' structure requires an alkylene group between phenylene and the -$NR^{46}R^{47}$ moiety. Therefore, the Examiner incorrectly states that Example 21 has X as methylene. The methylene referred to by the Examiner, links the piperidine and phenylene rings, while the X recited in Applicants' claimed structures links the piperidine and the -$NR^{46}R^{47}$ moiety.

Another significant distinction between the Takeuchi teaching and the presently claimed structure is that Applicants' structure has a terminal tertiary amine, -$NR^{46}R^{47}$. As noted above, Takeuchi's B ring is defined as "a nitrogen-containing saturated hetero-ring which may have a substituent on the nitrogen atom and which may have cross-linking" (Abstract and page 5, lines 1-2). A terminal tertiary amine is never specifically called for. For example, in describing the R^2 substituent present on the ring nitrogen atom (page 5, lines 15-35), Takeuchi defines R^2 as being "a hydrogen atom, a lower alkyl group, a lower alkenyl group, a lower alkynyl group, a cycloalkyl-lower alkyl group, an aralkyl group which may have a substituent, or a lower alkyl group substituted with a heterocyclic group which has 1 or 2 hetero atoms, which may have a substituent and which may be condensed" (page 5, lines 38-40).

Of the 66 compounds exemplified on pages 45-66, only one compound, Example 21, has a tertiary amine, -$N(CH_3)_2$. However, Example 21 is distinguishable over the presently claimed compounds for several reasons, as pointed out above. Examples 33, 34 and 35 illustrate primary amines, and none of the additional compounds shown on pages 52-55 depict a tertiary amine.

Therefore, even if one skilled in the art were to review the Takeuchi teaching relating to the core structure:



and the broad definition of B as being "a nitrogen-containing saturated hetero-ring which may have a substituent on the nitrogen atom and which may have cross-linking" as well as the broad definition of the R^2 substituent that may be present on the ring nitrogen atom (a hydrogen atom, a lower alkyl group, a lower alkenyl group, a lower alkynyl group, a cycloalkyl-lower alkyl

group, an aralkyl group which may have a substituent, or a lower alkyl group substituted with a heterocyclic group which has 1 or 2 hetero atoms, which may have a substituent and which may be condensed), they would have to pick and choose without any motivation or suggestion from Takeuchi, to select a piperidine ring as the nitrogen containing ring, add a non-hydrogen moiety at the carbon linking the ring to the carbamate, and link a tertiary amine to the nitrogen by means of an alkylene (optionally substituted with 1-3 -OH groups), alkylene where 1-3 carbons have been replaced by oxygen atom, or an -alkylene-phenylene-alkylene- (phenylene ring is optionally substituted with 1-2 -Cl or -F) linker, as is recited in the claims.

In conclusion, Applicants assert that a *prima facie* case of obviousness has not been established since Takeuchi does not suggest the invention as presently claimed. Applicants submit that the invention is patentable under 35 U.S.C. §103(a) and respectfully request withdrawal of the rejection.

III. CONCLUSION

The above arguments are submitted for the purpose of facilitating allowance of the Claims and a sincere effort has been made to place this application in condition for allowance. An early notice of allowance is earnestly requested. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney for Applicants.

Respectfully submitted,
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